



# Emergency department visits for acute asthma by adults who ran out of their inhaled medications

## Citation

Hasegawa, Kohei, Barry E. Brenner, Sunday Clark, and Carlos A. Camargo. 2014. "Emergency department visits for acute asthma by adults who ran out of their inhaled medications." Allergy and Asthma Proceedings 35 (3): e42-e50. doi:10.2500/aap.2014.35.3747. <http://dx.doi.org/10.2500/aap.2014.35.3747>.

## Published Version

doi:10.2500/aap.2014.35.3747

## Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:12406872>

## Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

## Share Your Story

The Harvard community has made this article openly available.  
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

# Emergency department visits for acute asthma by adults who ran out of their inhaled medications

Kohei Hasegawa, M.D., M.P.H.,<sup>1</sup> Barry E. Brenner, M.D., Ph.D.,<sup>2</sup> Sunday Clark, M.P.H., Sc.D.,<sup>3</sup> and Carlos A. Camargo, Jr., M.D., Dr.P.H.<sup>1</sup>

## ABSTRACT

*This study was designed to determine the percentage of asthma-related emergency department (ED) visits made by patients who recently ran out of their inhaled short-acting beta-agonists or inhaled corticosteroids and to characterize this understudied patient population. A secondary analysis was performed of data from four ED-based multicenter studies of acute asthma during 1996–1998 (n = 64 EDs). In each study, consecutive adult patients, aged 18–54 years, with acute asthma underwent a structured interview that assessed running out of inhaled medications. The analytic cohort comprised 1095 adults. Overall, 324 patients (30%; 95% confidence interval [CI], 27–32%) ran out of either of their inhaled beta-agonists or inhaled corticosteroids during the week before their index ED visit; 311 (28%; 95% CI, 26–31%) ran out of inhaled beta-agonists per se. Among a subset of 518 patients on inhaled corticosteroids, 55 patients (11%; 95% CI, 8–14%) ran out of inhaled corticosteroids. In the multivariable model, predictors of running out of an asthma medication were male sex, non-Hispanic black race, Hispanic ethnicity, no insurance, lower household income, and use of EDs as the preferred source of asthma prescriptions (all  $p < 0.05$ ). Among patients who ran out of medications, 49% (95% CI, 43–55%) ran out of inhaled beta-agonists and 72% (95% CI, 58–84%) ran out of inhaled corticosteroids, before onset of their acute asthma symptoms. In 1095 adult ED patients with acute asthma, we found that 30% ran out of their inhaled asthma medications before the ED visit. Asthma patients who ran out of medications had sociodemographic characteristics that may help with identification of preventable ED visits. Multifaceted strategies needed to ensure optimal use of inhaled medications are warranted.*

(Allergy Asthma Proc 35:e42–e50, 2014; doi: 10.2500/aap.2014.35.3747)

Asthma is an important public health problem in the United States. Asthma prevalence remains at historically high levels, affecting 26 million Americans in 2010.<sup>1</sup> Recent national estimates indicate that there are 2 million asthma emergency department (ED) visits each year.<sup>1–3</sup> This patient population is a cause for concern because most asthma-related ED visits represent a treatment or maintenance failure<sup>4,5</sup> and are deemed to be preventable through longitudinal disease management undertaken by both medical providers and the patient.<sup>6,7</sup> Furthermore, ED visits impose a heavy economic burden on health care spending as

much as five times more per visit than a typical outpatient office visit for asthma.<sup>8</sup>

Systematic evaluation of ED patients with acute asthma could identify reasons for the ED visits that go beyond acute asthma severity. For example, nonadherence with treatment is a contributor to the poor control in this patient population.<sup>9,10</sup> One form of nonadherence is “running out” of inhaled medications, such as inhaled  $\beta$ -agonists or inhaled corticosteroids. Studies have indicated that asthma patients commonly and significantly overestimate the remaining amount of asthma medication in metered-dose inhalers (MDIs).<sup>11–14</sup> Furthermore, with continued use of an MDI beyond the recommended number of doses, active medication delivery per actuation becomes inconsistent and unpredictable.<sup>15</sup> A potential consequence of running out of inhaled medications is suboptimal disease control and ED visits for acute asthma. Despite this likely clinical relevance for a major public health burden (asthma-related ED visits), there have been no studies, to date, that characterize this important patient population.

To address these gaps in current knowledge, we analyzed the data from several multicenter ED-based studies. The two objectives of the present analysis were (1) to determine the percentage of asthma-related ED visits made by adults who ran out of their inhaled short-acting  $\beta$ -agonists or inhaled corticosteroids be-

---

From the <sup>1</sup>Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, <sup>2</sup>Department of Emergency Medicine, University Hospitals Case Medical Center, Cleveland, Ohio, and <sup>3</sup>Department of Emergency Medicine, Weill Cornell Medical College, New York, New York

Funded by grant HL-63253 from the National Institutes of Health (Bethesda, Maryland), and by unrestricted grants from Glaxo Wellcome, Inc. (Research Triangle Park, North Carolina) and Monaghan Medical Corp. (Syracuse, New York); the present analysis was funded by an unrestricted grant from Teva (North Wales, Pennsylvania) CA Camargo has provided asthma-related consultation for Genentech, GlaxoSmithKline, Merck, Novartis, and Pfizer, and received a research grant from Novartis to study emergency care of acute asthma. The remaining authors have no conflicts of interest to declare pertaining to this article

Address correspondence to Kohei Hasegawa, M.D., M.P.H., Department of Emergency Medicine, Massachusetts General Hospital, 326 Cambridge Street, Suite 410, Boston, MA 02114

E-mail address: khasegawa1@partners.org

Copyright © 2014, OceanSide Publications, Inc., U.S.A.

fore the ED visit and (2) to identify characteristics of this understudied patient population. A better understanding these patients could help to improve their asthma management, close the chasms in asthma care, and reduce health care spending.

## METHODS

### Study Design and Participants

This study was a secondary analysis of the data from four ED-based multicenter prospective studies of acute asthma that were performed during 1996–1998, as part of the Multicenter Airway Research Collaboration.<sup>16–22</sup> Multicenter Airway Research Collaboration is part of the Emergency Medicine Network,<sup>23</sup> a research collaboration with >200 participating EDs. Using a standardized protocol, investigators at 64 North American EDs in 22 U.S. states and 4 Canadian provinces enrolled patients 24 hr/day for a median of 2 weeks. The Institutional Review Board at each of the 64 participating hospitals approved the study, and informed consent was obtained for all participants. All patients were managed at the discretion of the treating physician.

Inclusion criteria were adults aged 18–54 years with a history of asthma before the index ED visit and the ability to give informed consent. For the current analysis, patients were excluded if they did not use inhaled short-acting  $\beta$ -agonists during the past 4 weeks before their index ED visit or medication ran out status was not documented.

### Data Collection

The ED interview assessed patient demographics, socioeconomic status, asthma history, chronic asthma medications, medication ran-out status, and details of the current asthma exacerbation, including duration of symptoms. Data on respiratory rate, oxygen saturation, peak expiratory flow, ED course, and ED disposition were obtained by chart review. Follow-up interviews were performed by telephone 2 weeks after the ED visit. All forms were reviewed by site investigators before submission to the Emergency Medicine Network Coordinating Center in Boston, MA, where they underwent further review by trained personnel and then double data entry.

Median household income was estimated using home zip code. Peak expiratory flow was expressed as percentage of predicted value based on age, sex, height, and race/ethnicity.<sup>24</sup> Changes in peak expiratory flow are expressed as the absolute change in percent predicted (e.g., an improvement from 40% predicted to 70% predicted would be expressed as a change of 30%). Relapse was defined as any urgent visit to an ED or clinic for worsening of asthma during 2-week follow-up.

## Outcome Measures

The primary outcome measure was running out of an inhaled asthma medication, either inhaled short-acting  $\beta$ -agonists or inhaled corticosteroids, during the week before the index ED visit. Then, we further categorized this outcome by the medication class that ran out: inhaled short-acting  $\beta$ -agonists or inhaled corticosteroids.

### Statistical Analysis

Summary statistics at the patient levels are presented as proportions (with 95% confidence intervals [CIs]), means (with SDs), and medians (interquartile range). The unadjusted associations between patient characteristics and ran-out status were analyzed using chi-squared test, unpaired *t*-test, and Kruskal-Wallis test, as appropriate.

Multivariable logistic regression was performed to identify demographic and chronic asthma factors associated with the likelihood of running out of the medication, compared with not running out of the medication. Model variables were selected *a priori* based on clinical plausibility. These selected variables included age, sex, race/ethnicity, insurance, estimated household income, primary care provider status, hospitalization for asthma in the past year, and patient's preferred source of asthma medication prescriptions. We tested for two-way interaction by multiplying the two factors of interest and including an interaction term in the final multivariable model if the interaction was statistically significant ( $p < 0.05$ ).

We also examined the distributions of days from running out of each medication to the onset of the asthma exacerbation, stratified by medication class. All analyses used SAS Version 9.3 (SAS Institute, Cary, NC) and all odds ratios are presented with 95% CI.

## RESULTS

Of 1847 adult patients with acute asthma, we excluded patients who reported that they were not on inhaled short-acting  $\beta$ -agonists ( $n = 260$ ) and those with ran-out status not documented ( $n = 492$ ). After these exclusions, the analytic cohort comprised 1095 ED patients for acute asthma. The analytic cohort and patients with ran-out status not documented were similar in age and sex ( $p > 0.05$ ); but the analytic cohort had a lower proportion of black race (43% versus 54%;  $p < 0.001$ ). Of the 1095 ED patients, 324 patients (30%; 95% CI, 27–32%) ran out of either of their inhaled short-acting  $\beta$ -agonists or inhaled corticosteroids during the week before their index ED visit.

Unadjusted analysis of the associations between patient characteristics and ran-out status are shown in Table 1. Patients who ran out of their inhaled asthma medications were on average younger and had a sig-

Table 1 Characteristics of ED patients with acute asthma

	All Patients (n = 1095)	Ran out of Inhaled Medication (n = 324)	Did Not Run out of Inhaled Medication (n = 771)	p Value
Demographic factors				
Age (yr), mean $\pm$ SD	35 $\pm$ 10	34 $\pm$ 10	36 $\pm$ 10	0.003*
Male (%)	34	43	30	<0.001#
Race/ethnicity (%)				<0.001#
Non-Hispanic white	21	11	26	
Non-Hispanic black	54	64	49	
Hispanic	23	23	23	
Other	2	2	2	
Estimated household income, median (interquartile range)	27 879 (20,346–37,511)	26,953 (19,675–34,776)	28,961 (20,959–38,555)	0.003\$
Insurance status (%)¶				<0.001#
Private	30	21	34	
Medicaid	26	27	25	
Other public	11	10	11	
None	28	35	25	
Has primary care provider (%)	67	55	72	<0.001#
Current smoker (%)	33	40	31	0.004#
Chronic asthma factors				
Ever taken steroid medicine for asthma (%)	74	72	74	0.51#
Ever intubated for asthma (%)	18	21	17	0.21#
Admitted for asthma in past year (%)	35	32	36	0.51#
No. of ED visits in past year, median (interquartile range)	3 (1–5)	3 (1–6)	2 (0–5)	<0.00\$
Inhaled corticosteroids during past 4 wk (%)	48	44	49	0.14#
Days off from usual activities because of asthma during past year, median (interquartile range)	5 (0–20)	5 (1–20)	5 (0–21)	0.38\$
ED as preferred source of asthma prescriptions (%)	42	59	36	<0.001#
Acute asthma factors and clinical course				
Duration of symptoms, (%)¶				<0.001#
<24 hr	52	61	49	
>24 hr	46	37	49	
Initial respiratory rate (breaths/min), mean $\pm$ SD	24 $\pm$ 6	24 $\pm$ 5	24 $\pm$ 6	0.62*
Initial peak expiratory flow rate (% predicted), mean $\pm$ SD	48 $\pm$ 20	47 $\pm$ 18	49 $\pm$ 21	0.17*
Change in peak expiratory flow rate (% predicted), mean $\pm$ SD	24 $\pm$ 19	26 $\pm$ 18	24 $\pm$ 19	0.20*
Given steroid treatment (%)	72	68	74	0.01#
Admitted from ED (%)	23	17	26	0.03#
Relapse within 2 wk (%)	11	8	13	<0.001#

\*Unpaired t-test.

#Chi-square test.

\$Kruskal-Wallis test.

¶Percentages do not sum to 100% because of missing values.

ED = emergency department.

nificantly higher proportion of male sex and non-Hispanic black race compared with those who did not run out of medication (all,  $p < 0.01$ ). Markers of socioeconomic status (*e.g.*, estimated household income) were also associated with running out of an inhaled medication ( $p = 0.003$ ). Similarly, the proportion of patients with insurance or a primary care provider was significantly lower in those who ran out of their medications (both,  $p < 0.001$ ).

With regard to chronic asthma history, there were few significant differences between the groups. However, the number of asthma ED visits in the past year and the proportion of patients who reported the ED as their preferred source of asthma medication prescriptions were higher in those who ran out of their medications (both,  $p < 0.001$ ).

Although initial respiratory rate and peak expiratory flow of the two groups did not differ significantly, the patients who ran out of their inhaled medications had a higher proportion of acute onset of asthma exacerbation (*i.e.*,  $<24$  hours), compared with those who did not ( $p < 0.001$ ). Additionally, those who ran out had a lower proportion of hospital admission from the ED ( $p = 0.03$ ) and relapse within 2 weeks after ED discharge ( $p < 0.001$ ).

Table 2 summarizes patient characteristics according to inhaled medication. Among 1095 ED patients, 311 patients (28%; 95% CI, 26–31%) ran out of their inhaled short-acting  $\beta$ -agonists before the index ED visit. Among 518 patients on inhaled corticosteroids, 55 patients (11%; 95% CI, 8–14%) ran out of this medication. In addition, among 518 patients on inhaled short-acting  $\beta$ -agonists and inhaled corticosteroids, 42 patients (8%; 95% CI, 6–11%) ran out of both medications. Across the medication subgroups, the proportion of non-Hispanic black race, lower household income, no insurance or primary care provider, current smoking, and use of ED as the preferred source of asthma prescriptions was significantly higher in patients who ran out of their asthma medications (all,  $p < 0.05$ ).

Multivariable logistic regression modeling was performed to address the interrelations between many of these factors (Table 3). Overall, male sex, non-Hispanic black race, Hispanic ethnicity, no insurance, lower household income, and use of ED as the preferred source of asthma prescriptions were significantly associated with a higher chance of running out of their inhaled asthma medications (all,  $p < 0.05$ ). Most notably, non-Hispanic black patients and patients with no insurance had approximately two times higher odds of running out of their medications. Furthermore, across the subgroup analyses, no insurance remained as a significant predictor of running out of inhaled medications.

Figures 1 and 2 depict the days from running out of medications to the onset of acute asthma symptoms.

Interestingly, among those who ran out of their inhaled short-acting  $\beta$ -agonist, 49% (95% CI, 43–55%) ran out before the onset of symptoms. Among those who ran out of their inhaled corticosteroids, 72% (95% CI, 58–84%) ran out before the onset of symptoms.

## DISCUSSION

Our prospective cohort of 1095 ED patients with acute asthma showed that 30% of patients ran out of their asthma medications during the week before the ED visit. We found that male sex, non-Hispanic black race, markers of low socioeconomic status, and use of ED as the preferred source of asthma prescriptions were independently associated with a higher chance of running out of an inhaled asthma medication.

### Mechanisms of Running out of Asthma Medications

Medication nonadherence in asthma is well recognized, with adherence rates generally ranging from 30 to 70%.<sup>25,26</sup> The present study extends prior research by focusing on asthma-related ED visits made by patients who ran out of their inhaled medications. Defining the magnitude of this problem, along with risk factors, is essential to develop and implement targeted strategies in this high-risk population. There are many potential reasons why a significant proportion of patients ran out of their asthma medications before the ED visit. For example, an increased use of quick relievers during asthma exacerbations may have resulted in “running out of medication.” However, about one-half of these ED patients ran out of their inhaled short-acting  $\beta$ -agonists (and 70% ran out of their inhaled corticosteroids) before the onset of asthma exacerbation symptoms. Therefore, it is difficult to postulate that this mechanism fully explains the high percentage of adult ED patients who present to the ED with acute asthma.

Alternatively, our data indicate that personal health behavior is significantly associated with this form of medication nonadherence; indeed, ~60% of patients who ran out of their medications reported that they used EDs as the preferred source of asthma prescriptions. Furthermore, our findings, a shorter duration of asthma exacerbation symptoms and a lower rate of hospitalizations among these patients, might suggest heavier reliance on episodic symptom treatment in the ED for milder asthma exacerbations.

In addition, other nonbiological factors, such as less asthma education, a lack of personal action plans, and limited access to ambulatory health care and asthma specialists may contribute.<sup>27</sup> After the dissemination of National Asthma Education and Prevention Program guidelines in 1991, 1997, and 2007, the literature showed increases in the use of preventive asthma med-



Table 2 Characteristics of ED patients with acute asthma, according to medication type

	Inhaled Short-Acting $\beta$ -Agonists			Inhaled Corticosteroids		
	Ran out of Medication (n = 311)	Did Not Run out of Medication (n = 784)	p Value	Ran out of Medication (n = 55)	Did Not Run out of Medication (n = 463)	p Value
Demographic factors						
Age (yr), mean $\pm$ SD	34 $\pm$ 10	36 $\pm$ 10	0.002*	37 $\pm$ 10	38 $\pm$ 10	0.58*
Male (%)	44	30	<0.001#	35	29	0.35#
Race/ethnicity (%)			<0.001#			0.02#
Non-Hispanic white	12	26		11	27	
Non-Hispanic black	64	49		56	49	
Hispanic	22	23		27	22	
Other	2	2		6	2	
Estimated household income, median (interquartile range)	26,953 (19,765–35,139)	28,822 (20,907–38,064)	0.01\$	25,360 (19,288–32,677)	29,140 (21,724–39,412)	0.04\$
Insurance status (%)¶			<0.001#			0.005#
Private	21	34		16	37	
Medicaid	27	25		27	25	
Other public	9	11		11	13	
None	35	25		40	20	
Has primary care provider (%)	54	72	<0.001#	67	79	0.04#
Current smoker (%)	39	31	0.01#	45	26	0.003#
Chronic asthma factors						
Ever taken steroid medicine for asthma (%)	74	74	0.43#	76	88	0.04#
Ever intubated for asthma (%)	21	17	0.24#	25	25	0.94#
Admitted for asthma in past year (%)	32	36	0.48#	40	48	0.41#
No. of ED visits in past year, median (interquartile range)	3 (1–6)	2 (0–5)	<0.001	5 (1–10)	3 (1–6)	0.13\$
Inhaled corticosteroids during past 4 wk (%)	42	50	0.02#	100	100	—
Days off from usual activities because of asthma during past year, median (interquartile range)	6 (1–20)	5 (0–21)	0.48\$	5 (0–30)	8 (2–30)	0.45\$
ED as preferred source of asthma prescriptions (%)	59	38	<0.001#	45	31	0.03#
Acute asthma factors and clinical course						
Duration of symptoms, (%)¶			0.004#			0.001#
<24 hr	60	49		78	52	
>24 hr	38	49		20	46	
Initial respiratory rate (breaths/min), mean $\pm$ SD	24 $\pm$ 5	24 $\pm$ 6	0.51*	25 $\pm$ 6	25 $\pm$ 6	0.95*
Initial peak expiratory flow rate (% predicted), mean $\pm$ SD	46 $\pm$ 18	49 $\pm$ 21	0.10*	47 $\pm$ 19	49 $\pm$ 21	0.60*
Change in peak expiratory flow rate (% predicted), mean $\pm$ SD	26 $\pm$ 18	24 $\pm$ 19	0.21*	23 $\pm$ 20	22 $\pm$ 18	0.82*
Given steroid treatment (%)	68	74	0.02#	64	77	0.006#
Admitted from ED (%)	16	26	<0.001#	25	30	0.22#
Relapse within 2 wk (%)	8	13	<0.001#	4	14	<0.001#

\*Unpaired t-test.

#Chi-square test.

\$Kruskal-Wallis test.

¶Percentages do not sum to 100% because of missing values.

ED = emergency department.

Table 3 Multivariable model of factors associated with running out of inhaled asthma medication, overall and according to medication type

Variables*	Inhaled Medication		Inhaled Short-Acting $\beta$ -Agonists		Inhaled Corticosteroids	
	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value
Age, decile (yr)	0.86 (0.75–1.00)	0.052	<b>0.86 (0.74–1.00)</b>	<b>0.049</b>	1.01 (0.74–1.39)	0.94
Male sex	<b>1.44 (1.05–1.97)</b>	<b>0.02</b>	<b>1.54 (1.12–2.12)</b>	<b>0.08</b>	0.94 (0.60–1.10)	0.86
Race/ethnicity		<b>0.01</b>		<b>0.02</b>		<b>0.04</b>
Non-Hispanic white	1 (reference)		1 (reference)		1 (reference)	
Non-Hispanic black	<b>2.12 (1.35–3.32)</b>		<b>1.99 (1.26–3.13)</b>		2.86 (0.93–8.82)	
Hispanic	<b>1.68 (1.02–2.79)</b>		<b>1.53 (0.92–2.56)</b>		2.96 (0.89–9.79)	
Other	2.39 (0.77–7.44)		2.41 (0.77–7.51)		<b>7.64 (1.10–53.3)</b>	
Insurance status		<b>0.03</b>		<b>0.03</b>		<b>0.008</b>
Private	1 (reference)		1 (reference)		1 (reference)	
Medicaid	1.40 (0.94–2.09)		1.43 (0.95–2.15)		1.84 (0.74–4.59)	
Other public	1.26 (0.75–2.12)		1.16 (0.68–1.99)		1.55 (0.51–4.69)	
None	<b>1.58 (1.05–2.37)</b>		<b>1.58 (1.05–2.38)</b>		<b>2.21 (1.36–8.05)</b>	
Estimated household income (odds ratio per 10,000–U increase)	<b>0.87 (0.75–0.99)</b>	<b>0.04</b>	0.88 (0.77–1.02)	0.08	0.81 (0.60–1.10)	0.18
Has primary care provider	1.05 (0.71–1.55)	0.82	1.02 (0.69–1.52)	0.92	0.76 (0.32–1.82)	0.54
Admitted for asthma in past year	0.87 (0.64–1.19)	0.38	0.88 (0.64–1.20)	0.41	0.54 (0.29–1.02)	0.06
ED as preferred source of asthma prescriptions	<b>1.88 (1.31–2.68)</b>	<b>&lt;0.001</b>	<b>1.87 (1.30–2.69)</b>	<b>&lt;0.001</b>	1.23 (0.57–2.68)	0.60

Bold-face type results are statistically significant.

\*The multivariable model adjusts for the following patient and hospital characteristics: age, sex, race/ethnicity, insurance status, estimated household income, primary care provider status, hospital admission for asthma in past year, and ED as preferred source of asthma prescriptions. Testing for interactions among sex, insurance status, and primary care provider status did not indicate the presence of an effect modification; therefore, these interaction terms were not included in the final models. ED = emergency department.

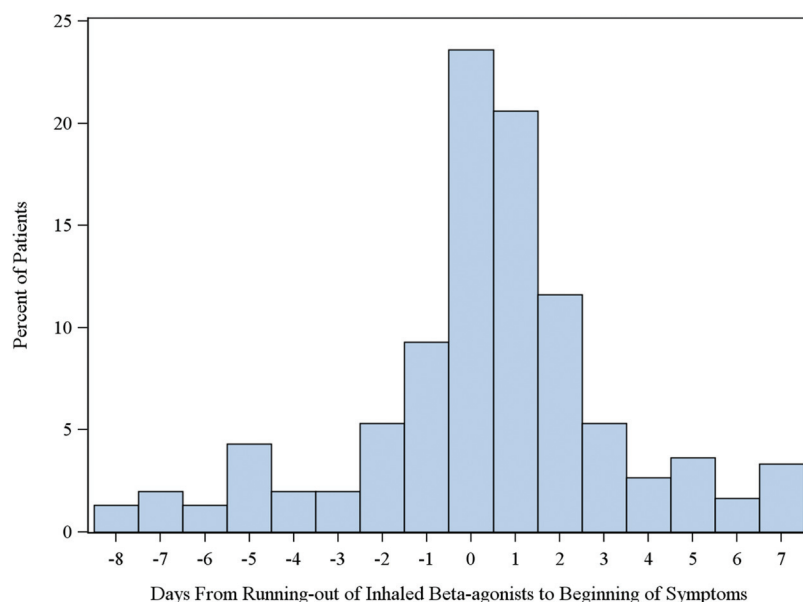
ications.<sup>28,29</sup> However, important aspects of the guidelines, such as asthma education and action plans, remain widely underused.<sup>30</sup> In addition, our national survey of 177 asthma centers indicated a suboptimal coordination of care between EDs and asthma centers,<sup>31</sup> which is particularly unfortunate given prior studies showing that interventions and treatment by asthma specialists are associated with decreased asthma-related ED visits<sup>32,33</sup> and that dedicated asthma centers have shown promise in reducing ED use.<sup>34,35</sup> Although the ED-to-specialist linkage has not materialized, these prior studies support optimism that adverse asthma outcomes can be prevented and the personal and public health burden can be reduced.

#### Underestimation of Patients Who Ran out of Medications

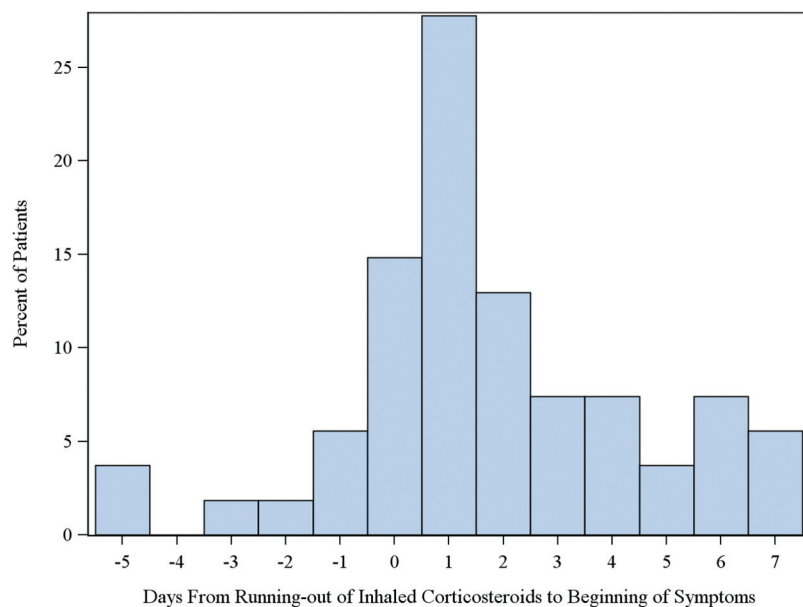
Although our data were gathered prospectively, questionnaire items regarding medication ran-out status were self-reported and there was no attempt to

verify the accuracy of the stated information. However, prior studies have reported that asthma patients overestimate the remaining amount of asthma rescue medications in MDIs; indeed, up to 40% of patients believed that they were taking their asthma medications when they activate an empty or nearly empty MDI.<sup>11,12</sup> Therefore, our study may have underestimated the magnitude of the asthma morbidity caused by running out of the inhaled medication.

With the current design of MDIs, it is not possible for an MDI to cease delivering a spray when the active drug has been depleted. MDIs continue to deliver a spray, which may not be within the labeled specifications for the active drug; the amount of drug in those additional actuations becomes inconsistent and unpredictable, with the amount of active drug eventually becoming negligible, a phenomenon known as “tail-off.”<sup>15</sup> Additionally, a growing number of literature has shown high error rates in patient’s ability to gauge doses remaining in their MDIs with various methods,



**Figure 1.** Days from running out of inhaled short-acting  $\beta$ -agonists to beginning of symptoms.



**Figure 2.** Days from running out of inhaled corticosteroids to beginning of symptoms.

such as the weight of the inhaler, the force, sounds, and taste of the actuation.<sup>14,36</sup> In addition, the only Food and Drug Administration–approved approach is for patients to keep track of doses as they use them; however, demanding this practice is impractical.<sup>13</sup> The incorrect use of asthma medications would likely lead to poor control of asthma symptoms and, potentially, ED visits for acute asthma. These data not only underscore the importance of patient education on the optimal use of asthma medications but also emphasize the importance of reliable means to monitor the contents of their MDIs.<sup>13</sup> Indeed, the latter was supported by the Food and Drug Administration’s Guidance for Industry to integrate dose-counting mechanisms into MDIs.<sup>37</sup>

### Disparities in Prevalence of Running out of Medications

We were also struck by the racial/ethnic and socioeconomic disparities for this type of medication nonadherence. Asthma patients at highest risk of running out of medications were non-Hispanic black patients and had no insurances and lower household income. These observations are consistent with prior studies showing less self-management education, lower inhaled corticosteroid use, and more limited access to preventive and specialist care among U.S. minority populations, which may lead to heavier reliance on episodic symptom treatment and an increased incidence of emergency asthma care in this population.<sup>38–41</sup>



Recent research has advanced our understanding of medication nonadherence in chronic conditions; it is a common problem reflecting a failure of the health care system and is understood as a variable behavior with intentional and unintentional causes.<sup>42</sup> Intentional nonadherence is the product of a decision informed by beliefs and preferences; unintentional nonadherence is linked to limitations in capacity of resources. Given that the causes of nonadherence are likely complex and multilevel, clinical strategies to address these disparities must therefore be multifaceted and target many aspects of asthma care.<sup>43,44</sup> The strategies should address the perceptual barriers limiting patients' motivation to persist with the inhaled medications by improving patient-provider communication about patient preference, asthma beliefs, and barriers to care. In addition, it is imperative to address the practical barriers influencing the ability to adhere to the treatment regimen (*e.g.*, not running out of inhaled medications) by improving access to longitudinal preventive care and refining asthma medication devices. For example, inclusion of dose-counting mechanisms as a standard feature of every MDI—one of the currently available measures—may help to ensure that patients receive accurate metered doses of asthma medication and to provide reliable information for when to replace an MDI,<sup>11,45</sup> thereby improving optimal use of medications and potentially reducing preventable ED visits for acute asthma.

### Limitations

Our study has several potential limitations. First, we analyzed multicenter data from ~15 years ago; therefore, our ability to extrapolate these inferences to the current asthma patient population may be limited. However, we note that, to date, there have been no other studies on ED patients who run out of their inhaled asthma medications. Therefore, we believe that our older data represent the best information available and will be helpful in health policy discussions about this underrecognized problem. Moreover, our data will assist the design of future studies to further explore this important issue in current asthma patients. Second, we did not analyze the outpatient management of these patients presenting with acute asthma, such as asthma self-management education and access to specialist care; these factors probably are associated with medication ran-out status. Furthermore, we have only sparse data on psychosocial problems and barriers to health care access of this high-risk population; these are areas for future investigation. Finally, the EDs that composed this sample were predominantly urban, teaching hospitals. This may make these results less generalizable to other clinical settings (*e.g.*, community hospitals). However, urban areas have disproportion-

ately high asthma morbidity, and it is in precisely this population for which targeted preventive measures are most urgently needed.

### CONCLUSION

By using interview data from 1095 adult ED patients with acute asthma, we found that 30% of patients ran out of their asthma medications before their ED visit. We also showed that male sex, non-Hispanic black race, markers of low socioeconomic status, and use of ED as the preferred source of asthma prescriptions were significantly associated with a higher chance of running out of their asthma medications. Our ability to extrapolate these results to the current asthma patient population may be limited. However, for researchers, our data represent the best information available and may assist in the design of future studies to further explore this understudied topic—in the current asthma population. Additionally, for policy makers, our findings underscore the importance of multifaceted strategies—*e.g.*, inclusion of dose-counting mechanisms as a standard feature of every MDI—to curb the asthma-related public health burden in an already-stressed health care system.

### REFERENCES

- Centers for Disease Control and Prevention. National surveillance of asthma: United States, 2001–2010. Available online at [www.cdc.gov/asthma/asthma.htm](http://www.cdc.gov/asthma/asthma.htm); accessed December 19, 2013.
- Barnett SB, and Nurmagambetov TA. Costs of asthma in the United States: 2002–2007. *J Allergy Clin Immunol* 127:145–152, 2011.
- American Lung Association. Trends in asthma morbidity and mortality. 2012. Available online at [www.lung.org/finding-cures/our-research/epidemiology-and-statistics-rpts.html](http://www.lung.org/finding-cures/our-research/epidemiology-and-statistics-rpts.html); accessed December 19, 2013.
- Coventry JA, Weston MS, and Collins PM. Emergency room encounters of pediatric patients with asthma: Cost comparisons with other treatment settings. *J Ambul Care Manage* 19:9–21, 1996.
- Carr W, Szapiro N, Heisler T, and Krasner MI. Sentinel health events as indicators of unmet needs. *Soc Sci Med* 29:705–714, 1989.
- Fuhlbrigge A, Carey VJ, Adams RJ, et al. Evaluation of asthma prescription measures and health system performance based on emergency department utilization. *Med Care* 42:465–471, 2004.
- Cloutier MM, Hall CB, Wakefield DB, and Bailit H. Use of asthma guidelines by primary care providers to reduce hospitalizations and emergency department visits in poor, minority, urban children. *J Pediatr* 146:591–597, 2005.
- Weiss KB, Sullivan SD, and Lyttle CS. Trends in the cost of illness for asthma in the United States, 1985–1994. *J Allergy Clin Immunol* 106:493–499, 2000.
- Krishnan JA, Riekert KA, McCoy JV, et al. Corticosteroid use after hospital discharge among high-risk adults with asthma. *Am J Respir Crit Care Med* 170:1281–1285, 2004.
- Williams LK, Pladevall M, Xi H, et al. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 114:1288–1293, 2004.

11. Wasserman RL, Sheth K, Lincourt WR, et al. Real-world assessment of a metered-dose inhaler with integrated dose counter. *Allergy Asthma Proc* 27:486–492, 2006.
12. Sheth K, Wasserman RL, Lincourt WR, et al. Fluticasone propionate/salmeterol hydrofluoroalkane via metered-dose inhaler with integrated dose counter: Performance and patient satisfaction. *Int J Clin Pract* 60:1218–1224, 2006.
13. Sander N, Fusco-Walkert SJ, Harder JM, and Chipps BE. Dose counting and the use of pressurized metered-dose inhalers: running on empty. *Ann Allergy Asthma Immunol* 97:34–38, 2006.
14. Holt S, Holt A, Weatherall MR, et al. Metered dose inhalers: A need for dose counters. *Respirology* 10:105–106, 2005.
15. Hess DR. Aerosol delivery devices in the treatment of asthma. *Respir Care* 53:699–723, 2008.
16. Silverman RA, Boudreaux ED, Woodruff PG, et al. Cigarette smoking among asthmatic adults presenting to 64 emergency departments. *Chest* 123:1472–1479, 2003.
17. Singh AK, Cydulka RK, Stahmer SA, et al. Sex differences among adults presenting to the emergency department with acute asthma. Multicenter Asthma Research Collaboration Investigators. *Arch Intern Med* 159:1237–1243, 1999.
18. Emerman CL, Woodruff PG, Cydulka RK, et al. Prospective multicenter study of relapse following treatment for acute asthma among adults presenting to the emergency department. MARC investigators. Multicenter Asthma Research Collaboration. *Chest* 115:919–927, 1999.
19. Barr RG, Woodruff PG, Clark S, and Camargo CA Jr. Sudden-onset asthma exacerbations: Clinical features, response to therapy, and 2-week follow-up. Multicenter Airway Research Collaboration (MARC) investigators. *Eur Respir J* 15:266–273, 2000.
20. Boudreaux ED, Clark S, and Camargo CA Jr. Telephone follow-up after the emergency department visit: Experience with acute asthma. On behalf of the MARC Investigators. *Ann Emerg Med* 35:555–563, 2000.
21. Zimmerman JL, Woodruff PG, Clark S, and Camargo CA. Relation between phase of menstrual cycle and emergency department visits for acute asthma. *Am J Respir Crit Care Med* 162:512–515, 2000.
22. Cydulka RK, Emerman CL, Rowe BH, et al. Differences between men and women in reporting of symptoms during an asthma exacerbation. *Ann Emerg Med* 38:123–128, 2001.
23. Emergency Medicine Network. Available online at [www.emnet-usa.org](http://www.emnet-usa.org); accessed February 11, 2014.
24. Hankinson JL, Odencrantz JR, and Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 159:179–187, 1999.
25. Horne R. Compliance, adherence, and concordance: Implications for asthma treatment. *Chest* 130(suppl):65S–72S, 2006.
26. Bender B, Milgrom H, and Rand C. Nonadherence in asthmatic patients: Is there a solution to the problem? *Ann Allergy Asthma Immunol* 79:177–185, 1997.
27. Tsai CL, Sullivan AF, Gordon JA, et al. Quality of care for acute asthma in 63 US emergency departments. *J Allergy Clin Immunol* 123:354–361, 2009.
28. Doerschug KC, Peterson MW, Dayton CS, and Kline JN. Asthma guidelines: An assessment of physician understanding and practice. *Am J Respir Crit Care Med* 159:1735–1741, 1999.
29. Rank MA, Liesinger JT, Ziegenfuss JY, et al. The impact of asthma medication guidelines on asthma controller use and on asthma exacerbation rates comparing 1997–1998 and 2004–2005. *Ann Allergy Asthma Immunol* 108:9–13, 2012.
30. Gibson PG, and Powell H. Written action plans for asthma: An evidence-based review of the key components. *Thorax* 59:94–99, 2004.
31. Sullivan AF, Schatz M, Wenzel SE, et al. A profile of U.S. asthma centers, 2006. *Ann Allergy Asthma Immunol* 99:419–423, 2007.
32. Vilar ME, Reddy BM, Silverman BA, et al. Superior clinical outcomes of inner city asthma patients treated in an allergy clinic. *Ann Allergy Asthma Immunol* 84:299–303, 2000.
33. Vollmer WM, O'Hollaren M, Ettinger KM, et al. Specialty differences in the management of asthma. A cross-sectional assessment of allergists' patients and generalists' patients in a large HMO. *Arch Intern Med* 157:1201–1208, 1997.
34. Battleman DS, Callahan MA, Silber S, et al. Dedicated asthma center improves the quality of care and resource utilization for pediatric asthma: A multicenter study. *Acad Emerg Med* 8:709–715, 2001.
35. Teach SJ, Crain EF, Quint DM, et al. Improved asthma outcomes in a high-morbidity pediatric population: Results of an emergency department-based randomized clinical trial. *Arch Pediatr Adolesc Med* 160:535–541, 2006.
36. Conner JB, and Buck PO. Improving asthma management: The case for mandatory inclusion of dose counters on all rescue bronchodilators. *J Asthma* 50:658–663, 2013.
37. U.S. Department of Health and Human Services. Guidance for industry: Integration of dose-counting mechanisms into MDI drug Products. Food and Drug Administration. Available online at [www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071731.pdf](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071731.pdf); accessed December 19, 2013.
38. Rand CS, Butz AM, Kolodner K, et al. Emergency department visits by urban African American children with asthma. *J Allergy Clin Immunol* 105:83–90, 2000.
39. Zoratti EM, Havstad S, Rodriguez J, et al. Health service use by African Americans and Caucasians with asthma in a managed care setting. *Am J Respir Crit Care Med* 158:371–377, 1998.
40. Schmalzing KB, Afari N, and Blume AW. Predictors of treatment adherence among asthma patients in the emergency department. *J Asthma* 35:631–636, 1998.
41. Hasegawa K, Tsugawa Y, Brown DF, and Camargo CA Jr. A population-based study of adults who frequently visit the emergency department for acute asthma: California and Florida, 2009–2010. *Ann Am Thorac Soc* 2013. (Epub ahead of print.)
42. Byrne M, Walsh J, and Murphy AW. Secondary prevention of coronary heart disease: Patient beliefs and health-related behaviour. *J Psychosom Res* 58:403–415, 2005.
43. Sabin BR, and Greenberger PA. Chapter 13: Potentially (near) fatal asthma. *Allergy Asthma Proc* 33(suppl 1a):S44–S46, 2012.
44. Canino G, McQuaid EL, and Rand CS. Addressing asthma health disparities: A multilevel challenge. *J Allergy Clin Immunol* 123:1209–1217, 2009.
45. Given J, Taveras H, Iverson H, and Lepore M. Prospective, open-label assessment of albuterol sulfate hydrofluoroalkane metered-dose inhaler with new integrated dose counter. *Allergy Asthma Proc* 34:42–51, 2013. □